CLAIMS

1. An antibody Fab' fragment, characterized in that the interchain cysteine of C_H1 has been replaced by another amino acid.
2. The antibody Fab' fragment of claim 1 that contains a modified hinge region.
3. The antibody Fab' fragment of claim 2 in which the hinge comprises or consists of any one of the sequences provided in SEQ ID Nos 1-14.
4. The antibody Fab' fragment of claim 2 and claim 3 in which the C_L interchain cysteine is covalently bonded to a cysteine in the hinge region.
5. An antibody Fab' fragment, characterized in that both the interchain cysteine of C_H1 and C_L have been replaced by another amino acid and an engineered cysteine in the light chain constant region is covalently bonded to a cysteine in the hinge region.
6. The antibody Fab' fragment of claim 5 in which the light chain constant region comprises or consists of any one of the sequences provided in SEQ ID Nos 16-20.
7. The antibody Fab' fragment of claim 6 in which the hinge comprises or consists of any one of the sequences provided in SEQ ID Nos 1-11.
8. An antibody Fab' fragment, characterized in that the interchain cysteine of C_L has been replaced by another amino acid.
9. The antibody Fab' fragment of claim 8 that contains a modified hinge region.
10. An antibody Fab fragment, characterized in that the C_H1 interchain cysteine has been replaced by another amino acid.
11. An antibody Fab fragment, characterized in that the C_L interchain cysteine has been replaced by another amino acid.
12. The antibody Fab or Fab' fragment of claims 1-11 where the interchain cysteine that has been replaced has been replaced by a non-thiol containing amino acid.
13. The antibody Fab or Fab' fragment of claim 12 wherein the non-thiol containing amino acid is serine.
14. The antibody Fab or Fab' fragment of claims 1 to 13 to which at least two effector molecules are attached.
15. The antibody Fab or Fab' fragment of claim 14 where an effector molecule is attached to a cysteine in the light chain constant region and/or a cysteine in the heavy chain constant region.
16. The antibody fragment of claim 15, wherein an effector molecule is attached to a cysteine in the light chain constant region and a cysteine in the heavy chain constant

region which would otherwise be linked to each other via a disulphide bond if the effector molecules were not attached.

17. The antibody fragment of claims 14-16 where an effector molecule is attached to the interchain cysteine of C_L or the interchain cysteine of C_H1 or an engineered cysteine in the light chain constant region, whichever is present in the fragment.
18. An antibody Fab' fragment according to claims 14-17 where an effector molecule is attached to each cysteine in the hinge region.
19. An antibody Fab' fragment according to claim 18 where an effector molecule is attached to a cysteine in the hinge which was covalently linked to the interchain cysteine of C_L prior to attachment of the effector molecules.
20. An antibody Fab' fragment according to claim 18 where an effector molecule is attached to a cysteine in the hinge which was covalently linked to an engineered cysteine in the light chain constant region prior to attachment of the effector molecules.
21. A method of producing an antibody Fab or Fab' fragment according to claims 14-20 comprising:
    a. Treating an antibody Fab or Fab' fragment according to any one of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or 13 with a reducing agent capable of generating a free thiol group in at least one cysteine of the heavy and/or light chain constant region and/or, where present, the hinge.
    b. Reacting the treated fragment with an effector molecule
22. The method of claim 21 where step (a) further comprises where present, reducing the covalent bond between the C_L interchain cysteine and a cysteine in the hinge region.
23. The method of claim 21 where step (a) further comprises where present, reducing the covalent bond between an engineered cysteine in the light chain constant region and a cysteine in the hinge region.
24. An antibody Fab or Fab' fragment to which two or more effector molecules are attached characterised in that the heavy chain in the fragment is not covalently bonded to the light chain and an effector molecule is attached to each of the interchain cysteines of C_L and C_H1.
25. The antibody Fab or Fab' fragment of claim 24 where at least one further effector molecule is attached to a cysteine in the light chain constant region and/or a cysteine in the heavy chain constant region.

26. The antibody fragment of claim 25, wherein an effector molecule is attached to a cysteine in the light chain constant region and a cysteine in the heavy chain constant region which would otherwise be linked to each other via a disulphide bond if the effector molecules were not attached.
27. An antibody Fab' fragment according to claim 26 that contains a modified hinge region.
28. The antibody Fab' fragment of claim 27 in which the hinge comprises or consists of any one of the sequences provided in SEQ ID Nos 1-14.
29. An antibody Fab' fragment according to claims 24-28 wherein an effector molecule is attached to at least one cysteine in the hinge region
30. A method of producing an antibody Fab or Fab' fragment according to claims 24-29 comprising:
    a. Treating an antibody Fab or Fab' fragment with a reducing agent capable of generating a free thiol group in at least the interchain cysteine of C_H1 and the interchain cysteine of C_L.
    b. Reacting the treated fragment with an effector molecule.
31. The antibody fragments of claims 1-30 where the interchain cysteine of C_L is at position 214 of the light chain and the interchain cysteine of C_H1 is at position 233 of the heavy chain.
32. The method according to claims 21 and 30 in which the reducing agent is a non-thiol based reductant.
33. The method according to claim 32 in which the reductant is a trialkylphosphine.
34. The method according to claim 33 in which the trialkylphosphine reductant is tris(2-carboxyethyl)phosphine (TCEP).
35. The method according to claim 33 in which the trialkylphosphine reductant is tris(3-hydroxypropyl)phosphine (THP).
36. The method according to claims 21 and 30 in which either or both of steps (a) and (b) are performed in the presence of a chelating agent.
37. The method according to claim 36 in which the chelating agent is EDTA.
38. The method according to claim 37 in which both steps (a) and (b) are performed in the presence of EDTA.
39. A mixture containing two or more antibody Fab or Fab' fragments, characterized in that the mixture is enriched for Fab or Fab' fragments in which the heavy chains in the fragments are not covalently bonded to the light chains, the fragments have two

or more effector molecules attached and at least one of said molecules is attached to a cysteine in the light chain or the heavy chain constant region.

40. The mixture of claim 39 in which greater than 50% of the mixture comprises a Fab' or Fab fragment in which the heavy chain in the fragment is not covalently bonded to the light chain, the fragment has two or more effector molecules attached and at least one of said molecules is attached to a cysteine in the light chain or the heavy chain constant region.
41. The antibody fragment of claims 14-31 and 39-40 wherein the effector molecule is PEG
42. A host cell expressing the antibody fragment of claims 1-13.
43. A pharmaceutical composition comprising an antibody fragment according to any of the preceding claims, together with one or more pharmaceutically acceptable excipients, diluents or carriers.